RESPONSE

I. Status of the Claims

No claims have been cancelled. No claims have been amended. No new claims have been added.

Claims 1-8 are therefore presently pending in the case. For the convenience of the Examiner, a clean copy of the pending claims is attached hereto as **Exhibit A**.

II. Oath/Declaration

The Action first objects to the oath or declaration as defective, as allegedly the citizenship of inventor number 3, Andrew Olson, is not provided. Applicants note for the record that a new declaration of Andrew Olson was submitted by Applicants on March 1, 2002. The new declaration was received at the PTO, as evidenced by the stamped postcard received by Applicants (**Exhibit B**). Applicants submit herewith a copy of the declaration of Andrew Olson that was filed on March 1, 2002, which is in compliance with 37 C.F.R. § 1.67(a), and which identifies the application by application number and filing date.

III. Rejection of Claims 1-8 Under 35 U.S.C. § 101

The Action first rejects claims 1-8 under 35 U.S.C. § 101, as allegedly lacking a patentable utility. Applicants respectfully traverse.

The present invention has a number of substantial and credible utilities, not the least of which is in diagnostic assays, as described in the specification, at least at page 10, line 28. As described in the specification from page 15, line 29 to page 16, line 2, the present sequence defines several coding single nucleotide polymorphisms - specifically, a G/A polymorphism at nucleotide position 343 of SEQ ID NO:1, which can result in a valine or isoleucine being present at corresponding amino acid position 115 of SEQ ID NO:2; and a C/T polymorphism at nucleotide position 868 of SEQ ID NO:1, which can result in a cysteine or arginine being present at corresponding amino acid position 290 of SEQ ID NO:2. As such polymorphisms are the basis for diagnostic assays such as forensic analysis, which does not require the

identification of a specific medical condition, and is undoubtedly a "real world" utility, the present sequences must in themselves be useful. It is important to note that the presence of more useful polymorphic markers for forensic analysis would not mean that the present sequences lack utility. As clearly set forth by the Federal Circuit in *Carl Zeiss Stiftung v. Renishaw PLC*, 20 USPQ2d 1101 (Fed. Cir. 1991):

> An invention need not be the best or only way to accomplish a certain result, and it need only be useful to some extent and in certain applications: "[T]he fact that an invention has only limited utility and is only operable in certain applications is not grounds for finding a lack of utility." *Envirotech Corp. v. Al George, Inc.*, 221 USPQ 473, 480 (Fed. Cir. 1984)

Just because other polymorphic sequences from the human genome have been described does not mean that the use of the presently described polymorphic markers for forensic analysis is not a specific utility.

Applicants respectfully point out that the presently described polymorphisms are useful in forensic analysis exactly as they were described in the specification as originally filed - specifically, to identify individual members of the human population based on the presence or absence of the described polymorphism. Simply because the use of these polymorphic markers might provide additional information on the percentage of particular subpopulations that contain one or more of these polymorphic markers would not mean that "additional research" is needed in order for these markers as they are presently described in the instant specification to be of use to forensic science. As stated above, using the polymorphic markers as described in the specification as originally field will definitely distinguish members of a population from one another. In the worst case scenario, each of these markers are useful to distinguish 50% of the population (in other words, the marker being present in half of the population). The ability to eliminate 50% of the population from a forensic analysis clearly is a real world, practical utility. Therefore, the present sequence clearly meets the requirements of 35 U.S.C. § 101.

The Action states that "further research" is needed "to identify or reasonably confirm a 'real world' context of use" for the claimed invention (Action at page 4). Applicants respectfully point out that, with regard to a "real world context of use", as opposed to the nebulous concept of a "real world context of use" expressed by the Examiner in this and previous Office Actions, Applicants have repeatedly detailed, in the response filed on March 1, 2002 ("Applicants' first response") to the First Office Action in this case

("the First Action"), which was mailed on December 3, 2001, and Applicants' response mailed on September 5, 2002 ("Applicants' second response") to the Second Office Action issued in this case ("the Second Action"), which was mailed on May 7, 2002, that nucleic acid sequences similar to those set forth in SEQ ID NO:1 are used throughout the biotechnology industry every day, for example in gene chip applications, as detailed below. Applicants are completely at a loss to understand how the Examiner can consider the biotechnology industry, an industrial sector that has a market capitalization of hundreds of billions of dollars, not to be a part of the "real world".

As previously set forth in Applicants first and second responses, evidence of the "real world" substantial utility of the present invention is further provided by the fact that there is an entire industry established based on the use of gene sequences or fragments from genes in a gene chip format. Perhaps the most notable gene chip company is Affymetrix. Affymetrix is clearly a "real world" company, as evidenced the fact that the United States Patent and Trademark Office has issued numerous U.S. Patents to Affymetrix covering gene chip technology, as exemplified by U.S. Patent Nos. 5,445,934, 5,556,752, 5,744,305, 5,837,832, 6,156,501 and 6,261,776. However, there are many companies which have, at one time or another, concentrated on the use of gene sequences or fragments, in gene chip and non-gene chip formats, for example: Gene Logic, ABI-Perkin-Elmer, HySeq and Incyte. In addition, two such companies (Agilent acquired by American Home Products and Rosetta acquired by Merck) were viewed to have such "real world" value that they were acquired by large pharmaceutical companies for significant sums of money. Given the widespread utility of such "gene chip" methods using non-biologically validated, *public domain* gene sequence information, there can be little doubt that the use of the presently described *novel* biologically validated coding sequence would have great utility in such DNA chip applications. The "real world" substantial industrial utility of gene sequences or fragments would, therefore, appear to be widespread and well established. Furthermore, compositions that enhance the utility of such DNA chips, such as the presently sequence, must in themselves be useful. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

Regarding whether "further research" would be required to practice the claimed invention, Applicants point out that nucleic acid sequences such as SEQ ID NO:1 are routinely used by companies

throughout the biotechnology sector **exactly** as it is presented in the Sequence Listing, without **any** further experimentation. Although information regarding the biological activity of a particular nucleic acid sequence might make it even more useful in such applications, this does not mean that the presently described nucleic acid sequences lack a specific utility. Once again, "[A]n invention need not be the best or only way to accomplish a certain result" (*Carl Zeiss Stiftung v. Renishaw PLC, supra*).

Additionally, as set forth in Applicants' first and second responses, a sequence is present in the leading scientific repository for biological sequence data (GenBank), and has been annotated by third party scientists *wholly unaffiliated with Applicants* as "Homo sapiens similar to epidermis specific serine protease" (GenBank accession number XM_093852). Given this Genbank annotation, it is clear that those skilled in the art would clearly believe that Applicants' sequence is a serine protease. The Action states that "(w)hile it is agreed that the Genbank entry submitted by Applicants is highly homologous to the claimed polynucleotide, there is no evidence of its function other than being annotated as similar to a (*sic*) epidermis specific serine protease" (Action at page 4; emphasis in original). To support this position, the Examiner again cites Broun *et al.* (Science *282*:1315-1317, 1998) and Van de Loo *et al.* (Proc. Natl. Acad. Sci. USA *92*:6743-6747, 1995) as teaching that prediction of function based on homology is unpredictable. However, as detailed in Applicants' first response, these papers cite only one example, microsomal oleate desaturase/oleate 12-hydroxylase, where function based on sequence homology proved to be incorrect. One example out of the **thousands** of predictions of function based on homology that exist in the art is hardly indicative of a high level of uncertainty, and thus does not support the alleged lack of utility.

Although Applicants need only make one credible assertion of utility to meet the requirements of 35 U.S.C. § 101 (*Raytheon v. Roper*, 220 USPQ 592 (Fed. Cir. 1983); *In re Gottlieb*, 140 USPQ 665 (CCPA 1964); *In re Malachowski*, 189 USPQ 432 (CCPA 1976); *Hoffman v. Klaus*, 9 USPQ2d 1657 (Bd. Pat. App. & Inter. 1988)), as a further example of the utility of the presently claimed polynucleotide, as described in the specification at least at page 2, lines 24-26, the present nucleotide sequences have a specific utility in "identification of protein coding sequence" and "mapping a unique gene to a particular chromosome". This is evidenced by the fact that SEQ ID NO:1 can be used to map the 5 coding exons

of the gene comprising the presently claimed sequence on chromosome 4 (present within a chromosome 4 clone; Genbank Accession Number AC104819; alignment and the first page from the Genbank report are presented in **Exhibit C**). Applicants respectfully remind the Examiner that only a minor percentage (2-4%) of the genome actually encodes exons, which in-turn encode amino acid sequences. The presently claimed polynucleotide sequence provides biologically validated empirical data (*e.g.*, showing which sequences are transcribed, spliced, and polyadenylated) that *specifically* define that portion of the corresponding genomic locus that actually encodes exon sequence, as described above. Equally significant is that the claimed polynucleotide sequence defines how the encoded exons are actually spliced together to produce an active transcript (*i.e.*, the described sequences are useful for functionally defining exon splice-junctions). Such biologically validated splice junctions are superior to splice junctions that may have been predicted from genomic sequence alone, and, as detailed in the specification, at least at page 10, lines 28-33, that "sequences derived from regions adjacent to the intron/exon boundaries of the human gene can be used to design primers for use in amplification assays to detect mutations within the exons, introns, splice sites (*e.g.*, splice acceptor and/or donor sites), *etc.*, that can be used in diagnostics and pharmacogenomics". Applicants respectfully submit that the practical scientific value of biologically validated, expressed, spliced, and polyadenylated mRNA sequences is readily apparent to those skilled in the relevant biological and biochemical arts.

Clearly, the present polynucleotide provides exquisite specificity in localizing the specific region of human chromosome 4 that contains the gene encoding the given polynucleotide, a utility not shared by virtually any other nucleic acid sequences. In fact, it is this specificity that makes this particular sequence so useful. Early gene mapping techniques relied on methods such as Giemsa staining to identify regions of chromosomes. However, such techniques produced genetic maps with a resolution of only 5 to 10 megabases, far too low to be of much help in identifying specific genes involved in disease. The skilled artisan readily appreciates the significant benefit afforded by markers that map a specific locus of the human genome, such as the present nucleic acid sequence. For further evidence in support of the Applicants' position, the Examiner is requested to review, for example, section 3 of Venter *et al.* (*supra at* pp. 1317-1321, including Fig. 11 at pp.1324-1325), which demonstrates the significance of expressed sequence

information in the structural analysis of genomic data. The presently claimed polynucleotide sequence defines a biologically validated sequence that provides a unique and specific resource for mapping the genome essentially as described in the Venter *et al.* article. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

Finally, the requirements set forth in the Action for compliance with 35 U.S.C. § 101 do not comply with the requirements set forth by the Patent and Trademark Office ("the PTO") itself for compliance with 35 U.S.C. § 101. While Applicants are well aware of the new Utility Guidelines set forth by the USPTO, Applicants respectfully point out that the current rules and regulations regarding the examination of patent applications is and always has been the patent laws as set forth in 35 U.S.C. and the patent rules as set forth in 37 C.F.R., not the Manual of Patent Examination Procedure or particular guidelines for patent examination set forth by the USPTO. Furthermore, it is the job of the judiciary, not the USPTO, to interpret these laws and rules. Applicants are unaware of any significant recent changes in either 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit that is in keeping with the new Utility Guidelines set forth by the USPTO. This is underscored by numerous patents that have been issued over the years that claim nucleic acid fragments that do not comply with the new Utility Guidelines. As examples of such issued U.S. Patents, the Examiner is invited to review U.S. Patent Nos. 5,817,479, 5,654,173, and 5,552,281 (each of which claims short polynucleotides), and recently issued U.S. Patent No. 6,340,583 (which includes no working examples), none of which contain examples of the "real-world" utilities that the Examiner seems to be requiring. As issued U.S. Patents are presumed to meet all of the requirements for patentability, including 35 U.S.C. §§ 101 and 112, first paragraph (see Section IV, below), Applicants submit that the present polynucleotides must also meet the requirements of 35 U.S.C. § 101. While Applicants understand that each application is examined on its own merits, Applicants are unaware of any changes to 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit, since the issuance of these patents that render the subject matter claimed in these patents, which is similar to the subject matter in question in the present application, as suddenly non-statutory or failing to meet the requirements of 35 U.S.C. § 101. Thus, holding Applicants to a different standard of utility would be arbitrary and capricious, and, like other

clear violations of due process, cannot stand.

For each of the foregoing reasons, as well as the reasons set forth in Applicants' first and second responses, Applicants submit that as the presently claimed nucleic acid molecules have been shown to have a substantial, specific, credible and well-established utility, the rejection of claims 1-8 under 35 U.S.C. § 101 has been overcome, and request that the rejection be withdrawn.

IV. Rejection of Claims 1-8 Under 35 U.S.C. § 112, First Paragraph

The Action next rejects claims 1-8 under 35 U.S.C. § 112, first paragraph, since allegedly one skilled in the art would not know how to use the invention, as the invention allegedly is not supported by a specific, substantial, and credible utility or a well-established utility. Applicants respectfully traverse.

Applicants submit that as claims 1-8 have been shown to have "a specific, substantial, and credible utility", as detailed in section III above, the present rejection of claims 1-8 under 35 U.S.C. § 112, first paragraph, cannot stand.

Applicants therefore request that the rejection of claims 1-8 under 35 U.S.C. § 112, first paragraph, be withdrawn.

V. Rejection of Claim 2 Under 35 U.S.C. § 112, Second Paragraph

The Action next rejects claim 2 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the invention.

The Action rejects claim 2 as allegedly indefinite based on the term "sequence" in relation to nucleic acid hybridization, since "(h)ybridization occurs only between molecules" (Action at page 6), and the term "the complement thereof", since this term is allegedly indefinite "for reasons of record" (Action at page 6). Applicants again respectfully point out that the skilled artisan would clearly understand how the nucleotide sequence could hybridize, within the parameters set forth in claim 2, and would also understand that the skilled artisan would understand the term "the complement" to refer to the complete complement of SEQ ID NO:1. More importantly, however, Applicants submit that the United States Patent and Trademark Office **itself** finds this **exact** language to meet the requirements of 35 U.S.C. § 112, second

paragraph, as evidenced at least by issued U.S. Patent Nos. 6,531,309, 6,511,840, 6,476,210, 6,465,632, 6,462,186, 6,448,388, 6,444,456, 6,444,153 and 6,403,784, each of which contains the **exact same language** complained of by the Examiner in the present case. As issued U.S. Patents are presumed to meet all of the requirements for patentability, including 35 U.S.C. § 112, second paragraph, Applicants submit that the present polynucleotides must also meet the requirements of 35 U.S.C. § 112, second paragraph. Holding Applicants to a different standard of definiteness would be arbitrary and capricious, and, like other clear violations of due process, cannot stand.

Applicants submit that, for the reasons discussed above, claim 2 clearly meets the requirements of 35 U.S.C. § 112, second paragraph. Applicants therefore request withdrawal of this rejection.

VI. Rejection of Claims 1, 5 and 8 Under 35 U.S.C. § 112, First Paragraph

The Action next rejects claims 1, 5 and 8 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse.

The Examiner seems to be requiring that the function of each of the members of the genus be known in order to satisfy the written description requirement. However, the Examiner's stated position completely misreads the written description requirement. The repeated citations of Broun *et al.* (*supra*) and Van de Loo *et al.* (*supra*), which were dealt with in Section III, above, as well as the citation of Seffernick *et al.* (J. Bacteriol. *183*:2405-2410, 2001), for the proposition that changes in protein sequence can lead to changes in protein function, are **completely irrelevant** to the present question of compliance with 35 U.S.C. § 112, first paragraph. As set forth in Applicants' second response, the relevant section of the written description guidelines is herein reproduced with numbers corresponding to the ways in which the written description requirement can be satisfied: (1) by actual reduction to practice, (2) reduction to drawings, or (3) by disclosure of relevant, identifying characteristics, i.e., (4) structure or other physical and/or chemical properties, (5) by functional characteristics coupled with a known or disclosed correlation between function and structure, or (6) by a combination of such identifying characteristics. Thus, the

written description requirements can be satisfied by (1), (2), or (3), and part (3) can be satisfied by (4), (5), or (6). Applicants submit that claim 1 provides "structure or other physical or chemical properties", specifically, the **nucleotide sequence itself**. There is **no requirement** within section (4) for functional characteristics, this being included in sections (5) and (6) **only**. Thus, since claims 1, 5 and 8 satisfy section (3) by satisfying section (4), claims 1, 5 and 8 **must** meet the written description requirement.

As set forth in Applicants' first and second responses, the Federal Circuit has held that an adequate description of a chemical genus "requires a precise definition, such as by structure, formula, chemical name or physical properties" sufficient to distinguish the genus from other materials. *Fiers v. Sugano*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993; "*Fiers*"). *Fiers* goes on to hold that the "application satisfies the written description requirement since it sets forth the . . . nucleotide sequence" (*Fiers* at 1607). In other words, provision of a structure and formula - the nucleotide sequence - renders the application in compliance with 35 U.S.C. § 112, first paragraph. Importantly, the Action **admits** that claims 1, 5 and 8 do in fact include a distinguishing feature, specifically, that the nucleic acid molecule must include "at least 24 consecutive nucleotides of the polynucleotide of SEQ ID NO:1" (Action at page 7). Applicants respectfully point out that this is **all that is required** of claims 1, 5 and 8 to meet the written description requirement of 35 U.S.C. § 112, first paragraph.

For each of the foregoing reasons, as well as the reasons set forth in Applicants' first and second response, Applicants submit that the rejection of claims 1, 5 and 8 under 35 U.S.C. § 112, first paragraph, has been overcome, and request that the rejection be withdrawn.

VII. Rejection of Claims 1, 5 and 8 Under 35 U.S.C. § 112, First Paragraph

Claims 1, 5 and 8 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that is not described in the specification in such a way as to enable one skilled in the art to make and/or use the claimed invention. Applicants respectfully traverse.

The Action states that "this enablement rejection was applied due to the lack of information as to how one of skill in the art can reasonably make and use the polynucleotides, as encompassed by the claims" (Action at page 9; emphasis in original). The Action seems to contend that the specification provides

insufficient guidance regarding the biological function or activity of certain of the claimed compositions. As set forth in Section VI, above, the repeated citations of Broun *et al.* (*supra*) and Van de Loo *et al.* (*supra*) and Seffernick *et al.* (*supra*), for the proposition that changes in protein sequence can lead to changes in protein function, are once again **completely irrelevant** to the present question of compliance with 35 U.S.C. § 112, first paragraph. Importantly, such an enablement standard conflicts with established patent law. As discussed *In re Brana,* 34 USPQ2d 1436 (Fed. Cir. 1995; "*Brana*"), the Federal Circuit admonished the P.T.O. for confusing "the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption". *Brana* at 1442.

The Examiner states that the present invention could not be practiced without "undue experimentation" (Action bridging pages 10 and 11). However, it is important to remember that in assessing the question of whether undue experimentation would be required in order to practice the claimed invention, the key term is "undue", not "experimentation". *In re Angstadt and Griffin*, 190 USPQ 214 (CCPA 1976). In *In re Wands* (8 USPQ 2d 1400 (Fed. Cir. 1988); "*Wands*"), the P.T.O. took the position that the applicant failed to demonstrate that the disclosed biological processes of immunization and antibody selection could reproducibly result in a useful biological product (antibodies from hybridomas) within the scope of the claims. In its decision overturning the P.T.O.'s rejection, the Federal Circuit found that Wands' demonstration of success in four out of nine cell lines screened was sufficient to support a conclusion of enablement. The court emphasized that the need for some experimentation requiring, *e.g.*, production of the biological material followed by routine screening, was not a basis for a finding of non-enablement, stating:

> Disclosure in application for the immunoassay method patent does not fail to meet enablement requirement of 35 USC 112 by requiring 'undue experimentation,' even though production of monoclonal antibodies necessary to practice invention first requires production and screening of numerous antibody producing cells or 'hybridomas,' since practitioners of art are prepared to screen negative hybridomas in order to find those that produce desired antibodies, since in monoclonal antibody art one 'experiment' is not simply screening of one hybridoma but rather is entire attempt to make desired antibody, and since record indicates that amount of effort needed to obtain desired antibodies is not

> excessive, in view of Applicants' success in each attempt to produce antibody that satisfied all claim limitations.

Wands at 1400. Thus, the need for some experimentation does not render the claimed invention unpatentable under 35 U.S.C. § 112, first paragraph. Indeed, a considerable amount of experimentation may be permissible if such experimentation is routinely practiced in the art. *In re Angstadt and Griffin, supra*; *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991).

Applicants point out that significant commercial exploitation of nucleic acid sequences requires no more information than the nucleic acid sequence itself. Applications ranging from gene expression analysis or profiling (utilizing, for example, arrays of short, overlapping or non-overlapping, oligonucleotides and DNA chips, as described in Section III, above) to chromosomal mapping (utilizing, for example, short oligonucleotide probes or full length DNA sequences, as described in Section III, above) are practiced utilizing nucleic acid sequences and techniques that are well-known to those of skill in the art. The widespread commercial exploitation of nucleic acid sequence information points to the level of skill in the art, and the enablement provided by disclosures such as the present specification, which include specific nucleic acid sequences and guidance regarding the various uses of such sequences.

The Action questions the teaching and guidance in the specification for certain aspects of the present invention. However, as discussed above, this requirement is completely misplaced. There is sufficient knowledge and technical skill in the art for a skilled artisan to be able to make and use the claimed DNA species in a number of different aspects of the invention entirely without further details in a patent specification. For example, it is not unreasonable to expect a Ph.D. level molecular biologist to be able to use the disclosed sequence to design oligonucleotide probes and primers and use them in, for example, PCR based screening and detection methods to obtain the described sequences and/or determine tissue expression patterns. Nevertheless, the present specification provides highly detailed descriptions of techniques that can be used to accomplish many different aspects of the claimed invention, including recombinant expression, site-specific mutagenesis, *in situ* hybridization, and large scale nucleic acid screening techniques, and properly incorporates by reference a montage of standard texts into the specification, such as Sambrook *et al.* (*Molecular Cloning, A Laboratory Manual*) and Ausubel *et al.*

(*Current Protocols in Molecular Biology*) to provide even further guidance to the skilled artisan. Incorporation of material into the specification by reference is proper. *Ex parte Schwarze*, 151 USPQ 426 (PTO Bd. App. 1966). The § 112, first paragraph rejection is thus *prima facie* improper:

> As a matter of patent office practice, then, a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

In re Marzocchi & Horton, 169 USPQ 367, 369 (CCPA 1971), emphasis as in original. In any event, an alleged lack of express teaching is insufficient to support a first paragraph rejection where one of skill in the art would know how to perform techniques required to perform at least one aspect of the invention. As a matter of law, it is well settled that a patent need not disclose what is well known in the art. *In re Wands, supra.* In fact, it is preferable that what is well known in the art be omitted from the disclosure. *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81 (Fed. Cir. 1986). As standard molecular biological techniques are routine in the art, such protocols do not need to described in detail in the specification.

Furthermore, a specification "need describe the invention only in such detail as to enable a person skilled in the most relevant art to make and use it." *In re Naquin*, 158 USPQ 317, 319 (CCPA 1968); emphasis added. The present claims are thus enabled as they are supported by a specification that provides sufficient description to enable the skilled person to make and use the invention as claimed.

As detailed above, and in the previous response, all aspects of the enablement rejection under 35 U.S.C. § 112, first paragraph have been overcome. Applicants therefore respectfully request that the rejection be withdrawn.

VIII. Conclusion

The present document is a full and complete response to the Action. In conclusion, Applicants submit that, in light of the foregoing remarks, the present case is in condition for allowance, and such

favorable action is respectfully requested. Should Examiner Ramirez have any questions or comments, or believe that certain amendments of the claims might serve to improve their clarity, a telephone call to the undersigned Applicants' representative is earnestly solicited.

Respectfully submitted,

March 31, 2003
Date

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24231
PATENT TRADEMARK OFFICE

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Exhibit A

Clean Version of The Pending Claims in U.S. Patent Application Ser. No. 09/854,844

1. An isolated nucleic acid molecule comprising at least 24 contiguous bases of nucleotide sequence from SEQ ID NO:1.

2. An isolated nucleic acid molecule comprising a nucleotide sequence that:

(a) encodes the amino acid sequence shown in SEQ ID NO:2; and

(b) hybridizes under highly stringent conditions to the nucleotide sequence of SEQ ID NO:1 or the complement thereof.

3. An isolated nucleic acid molecule according to Claim 1 wherein said nucleotide sequence is a cDNA sequence.

4. An isolated nucleic acid molecule according to Claim 3 encoding the amino acid sequence described in SEQ ID NO:2.

5. A recombinant expression vector comprising the isolated nucleic acid molecule of claim 1.

6. The recombinant expression vector of claim 5, wherein said isolated nucleic acid molecule encodes the amino acid sequence of SEQ ID NO:2.

7. The recombinant expression vector of claim 6, wherein said isolated nucleic acid molecule comprises the nucleotide sequence of SEQ ID NO:1.

8. A host cell comprising the recombinant expression vector of claim 5.

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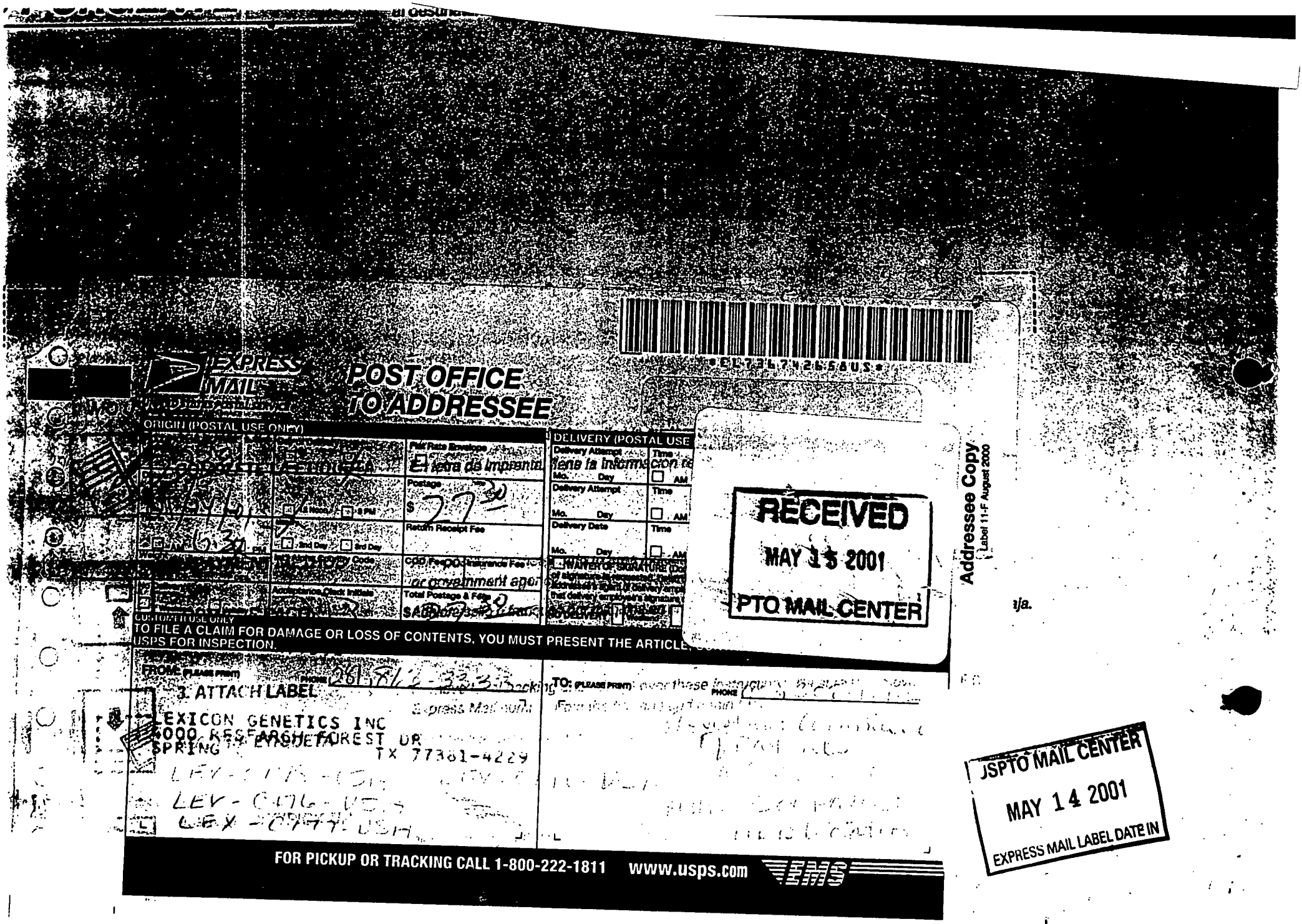
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Score = 766 bits (386), Expect = 0.0
Identities = 390/392 (99%)
Strand = Plus / Plus

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Sbjct: 46608 ctaacactatacacagagtaggcactgtagctgaagctgttgcttgcatacagggctggg 46667


Query: 950   aagagaatgcatggagatttagtcccaggggcagagaactcacaggagagccactgctaa 1009
              |||||||||||||||||||||||||||||||| ||||||||||||||||||||||||
Sbjct: 46668 aagagaatgcatggagatttagtcccaggggcagataactcacaggagagccactgctaa 46727


Query: 1010  ccctgggtgactttatttacaatttgaaatga 1041
              |||||||||||||||||||||||||||||||
Sbjct: 46728 ccctgggtgactttatttacaatttgaaatga 46759
```

Score = 524 bits (264), Expect = e-146
Identities = 265/266 (99%)
Strand = Plus / Plus

```
Query: 216   gacctggactacttttttcatatactgtgtggctaggatcgattacagtaggtgactcaag 275
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 37400 gacctggactacttttttcatatactgtgtggctaggatcgattacagtaggtgactcaag 37459


Query: 276   gaaacgtgtgaagtactacgtgtccaaaatcgtcatccatcccaagtaccaagatacaac 335
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 37460 gaaacgtgtgaagtactacgtgtccaaaatcgtcatccatcccaagtaccaagatacaac 37519


Query: 336   ggcagacrtcgccttgttgaaactgtcctctcaagtcaccttcacttctgccatcctgcc 395
              ||||||| ||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 37520 ggcagacgtcgccttgttgaaactgtcctctcaagtcaccttcacttctgccatcctgcc 37579


Query: 396   tatttgcttgcccagtgtcacaaagcagttggcaattccacccttttgttgggtgaccgg 455
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 37580 tatttgcttgcccagtgtcacaaagcagttggcaattccacccttttgttgggtgaccgg 37639


Query: 456   atggggaaaagttaaggaaagttcag 481
              |||||||||||||||||||||||||
Sbjct: 37640 atggggaaaagttaaggaaagttcag 37665
```

Score = 345 bits (174), Expect = 3e-92
Identities = 174/174 (100%)
Strand = Plus / Plus

```
Query: 479   cagatagagattaccattctgcccttcaggaagcagaagtacccattattgaccgccagg 538
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 38366 cagatagagattaccattctgcccttcaggaagcagaagtacccattattgaccgccagg 38425


Query: 539   cttgtgaacagctctacaatcccatcggtatcttcttgccagcactggagccagtcatca 598
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 38426 cttgtgaacagctctacaatcccatcggtatcttcttgccagcactggagccagtcatca 38485


Query: 599   aggaagacaagatttgtgctggtgatactcaaaacatgaaggatagttgcaagg 652
              ||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 38486 aggaagacaagatttgtgctggtgatactcaaaacatgaaggatagttgcaagg 38539
```

Score = 322 bits (162), Expect = 4e-85
Identities = 169/171 (98%), Gaps = 1/171 (0%)
Strand = Plus / Plus

```
Query: 47    tctc-agtgtgtgggcaacctgtatactccagccgcgttgtaggtggccaggatgctgct 105
             |||| ||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 35041 tctctagtgtgtgggcaacctgtatactccagccgcgttgtaggtggccaggatgctgct 35100


Query: 106   gcagggcgctggccttggcaggtcagcctacactttgaccacaactttatctatggaggt 165
             ||||||||||||||||||||||||||||||||||||||||||||||||||| |||||||
Sbjct: 35101 gcagggcgctggccttggcaggtcagcctacactttgaccacaactttatctgtggaggt 35160


Query: 166   tccctcgtcagtgagaggttgatactgacagcagcacactgcatacaaccg 216
             |||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 35161 tccctcgtcagtgagaggttgatactgacagcagcacactgcatacaaccg 35211
```

Score = 103 bits (52), Expect = 2e-19
Identities = 52/52 (100%)
Strand = Plus / Plus

```
Query: 1     atgggccctgctggctgtgccttcacgctgctccttctgctggggatctcag 52
             ||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 32425 atgggccctgctggctgtgccttcacgctgctccttctgctggggatctcag 32476
```